REMARKS

According to the above amendments, claim 43 has been amended. Claims 43-67 remain in this application with claims 49 and 57-67 presently withdrawn from further consideration as being drawn to a non-elected invention. Thus, claims 43-48 and 50-56 are currently being examined. No claim has been allowed.

Withdrawal of the rejection of claims 43-48 and 50-56 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement is gratefully acknowledged.

Claim Rejection - 35 USC § 112

Enablement

The Examiner has retained the rejection of claims 43-48 and 50-56 as not being fully enabled. Thus, the Examiner has maintained the position that the claims are only enabled for making retroviral particles using specific packaging cells containing specific genes and the passenger peptide being a specific peptide that binds to a specific cell type. The Examiner further maintains that the level of predictability based on the prior art is in question, in particular in relation to the size of the passenger peptide binding moiety, viral tropism determined by new contacts between viruses and cells, potential immune/inflammatory responses to the particles, cross interaction between the passenger peptide and a receptor affecting altered tropism of a viral particle.

Note that claim 43 has been amended to clarify that the

virus particle is an enveloped virus particle which uses an envelope that cannot naturally bind the cells of the species being targeted. Note, for example, in the examples, the ecotropic envelope is used because it only naturally binds to mouse cells and not human cells. However, when the ecotropic envelope includes the SCF molecule, it can then bind to human cells, but only those expressing the SCF receptor.

The above-described feature in the amended claims further qualifies the "first cell binding activity". Further support is found on page 8, lines 1-8 of the present application defining the natural host cell range of the virus. It is believed that the amendment to claim 43 addresses the Examiner's concerns regarding viral tropism and explains why the particles would not bind to other cells.

In relation to the Examiner's belief that potential immunogenicity of virus particles renders non-retroviruses non-enabled, it is not clear how a possible side effect of the therapy renders the invention not enabled. All "things", be they pharmaceutical compounds, antibodies, viruses, foodstuffs, etc. have the potential to be immunogenic, based on the molecules that they present to the immune system. The working of the invention would not necessarily be influenced by an immune response, and the presence of data for enveloped retroviruses that does not appear to have been affected by an immune response demonstrates that other enveloped viruses would similarly be capable of

functioning.

Various viruses have been used in gene therapy work including retroviruses, adenoviruses, adeno-associated viruses and herpes simplex viruses, the immunogenicity of the viruses and their envelopes are comparable in that work as in the current invention. The only key difference in the possible immunogenicity of the virus particles of the current invention is the passenger peptide. A skilled artisan seeking to include a passenger peptide in a virus particle surface will previously have investigated that peptide by itself including potential immunogenicity. Accordingly, one skilled in the art would appreciate that highly immunogenic peptides could potentially still be immunogenic when displayed on a virus particle envelope.

There is nothing unexpected regarding potential immune responses to virus particles and furthermore, such an immune response does not influence whether the invention is enabled for any virus or passenger peptide.

There is no reason, particularly in light of the above discussion, why a skilled person who works with viruses as possible gene transfer and targeting constructs would not be able to use the methods described in the application to express peptides for inclusion in virus particle envelopes.

In view of the amendments to claim 43 and the above remarks, reconsideration and withdrawal of this rejection is respectfully requested.

Indefiniteness

Claims 43-48 and 50-56 are newly rejected under 35 USC § 112, second paragraph, as being indefinite because of certain amendments previously presented, it being the Examiner's view that it is unclear what is encompassed by the phrase "passenger peptide-binding moiety". It is believed that this term is adequately defined in the specification (see, for example, page 6, lines 7-8) as a membrane-bound peptide moiety and as a peptide with a binding moiety expressed by a viral packaging cell that it is incorporated into the viral particle during viral budding (page 8, lines 17-19). Applicant believes that it is clear from normal usage of the term "passenger" that the passenger is something not normally found in that environment and carried along by a carrier. In this case, the "passenger" is a peptide not normally found in the viral particle.

Accordingly, applicant believes that support is found in the specification for using the phrase in question which gives it sufficient definiteness and clarity that the claim complies with 35 USC § 112, second paragraph. Reconsideration and withdrawal of this rejection is respectfully requested.

Claim Rejection - 35 USC § 102

The withdrawal of the rejection of claims 43-48 and 54-56 under 35 USC § 102(b) as being anticipated by Yajima et al is gratefully acknowledged.

Claims 43-46 and 54-56 have been newly rejected under 35 USC

§ 102(b) as being anticipated Soong et al (Soong et al., Molecular breeding of viruses.25(4):436-9, 2000). Soong et al is deemed to teach a method of breeding viruses with altered tropism without the use of a fused viral envelope protein. This rejection is respectfully traversed.

In this regard, claim 43 has been amended to specify that the passenger peptide is a heterologous peptide, i.e., one not derived from the virus or packaging cell in which it is to be displayed.

Soong *et al* describes a shuffling method for altering the viral genome in a form of accelerated evolution. Soong does not describe the synthesis of new viral particles by having a packaging cell express a peptide foreign to the virus such that the peptide is incorporated into the packaging cell membrane and subsequently into the viral envelope when viral budding occurs.

The Examiner has maintained that the "evolved" viral nucleic acid encoding an envelope protein is a "passenger peptide binding moiety". The applicant cannot agree with this view. As discussed above in relation to the other rejections, the passenger peptide is not a viral envelope protein (either natural or mutated). The passenger peptide is a peptide that bonds to a specific target molecule expressed only on the target cells of interest.

In view of the above, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claim Rejection - 35 USC § 103

The withdrawal of earlier rejections of claims 51 and 52-53 under 35 USC § 103 is gratefully acknowledged.

It is noted that, by the present Action, claims 43, 48, 50 and 51 have been rejected under 35 USC § 103(a) as being unpatentable over Soong et al, taken with Dropulic et al (USPN 6,114,141), previously cited. This rejection is respectfully traversed.

With respect to this rejection, claim 43 has been amended to specify that the passenger peptide is incorporated into the packaging cell membrane. Furthermore, as discussed above, Soong does not describe the passenger peptide as being heterologous. In addition, it is clear that Dropulic does not describe the expression of such heterologous proteins so as to be incorporated into the viral particle *via* the envelope formed by building.

Given the diversity, there is no reason to combine the teachings of these two documents. Soong is directed specifically to evolution of viral genes – there is no indication that a skilled person may want to add new heterologous genes – hence there is no incentive to combine these two documents.

Furthermore, the method of Soong is not readily adapted for dealing with different viruses or proteins. Soong requires a recombination process of evolution to be conducted each time a new final product is required. The current method allows different viruses to be replicated in the same packaging cell

line in order to get different viruses with the same passenger peptide in the envelope.

Additionally, it is of interest that the inventor has also advised us that the use of recombination in gene therapy vectors is not viable ("completely taboo" being his exact words) on the basis that you do not want your vectors recombining. He also informed us that gene therapy vectors specifically have recombining sequences removed from their genomes.

Accordingly, there is no reason why the skilled person would adapt Soong to form a gene therapy vector. Reconsideration and withdrawal of this rejection is respectfully requested.

It is further noted that claims 43, 48, 52 and 53 have been newly rejected under 35 USC § 103(a) as being unpatentable over Soong et al taken with Guber et al (USPN 5,691,177). This rejection is also respectfully traversed.

In this regard, it is noted that Guber '177 is quite similar to Dropulic, the only difference being that the references disclose different cytotoxic agents. This being the case, it is believed that the remarks pertinent to the combination of Soong et al and Dropulic apply equally to the combination of Soong et al and Guber et al; and for these reasons, it is believed that the present claims patentably distinguish over the combination of Soong and Guber as well.

Finally, it is noted that claims 43 and 47 have been newly rejected under 35 USC § 103(a) as being unpatentable over Soong

et al, taken with Yajima et al (Retroviral vector targeting human cells via c-Kit-stem cell factor interaction. *Hum Gene Ther.* 9(6): 779-87, 1998). This rejection is respectfully traversed.

Soong et al is believed to have been adequately distinguished. Yajima, on the other hand, does not describe enveloped viruses containing heterologous peptides derived from packaging cells at all, but describes a chimeric protein to a non-chimera and it is therefore believed that one skilled in the art would not be led to combine these documents nor would such a combination remove an inventive step from the present claims.

In view of the above amendments, taken together with the explanatory remarks herein, the Examiner is respectfully requested to withdraw the present rejections and allow the claims.

Should minor issues remain which, in the opinion of the Examiner, could be resolved by telephone interview, the Examiner is invited to contact the undersigned attorney at his convenience to discuss and hopefully resolve same.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Amendment in response to the Official Action of June 5, 2007 and a Transmittal Letter in application Serial No. 10/520,745, filed on August 22, 2005, of Colin M. Casimir, entitled "METHODS OF MAKING VIRAL PARTICLES HAVING A MODIFIED CELL BINDING ACTIVITY AND USES THEREOF" are being sent by facsimile transmission to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, postage prepaid, on August 6, 2007.

Barbara L. Davis
on behalf of C. G. Mersereau
Attorney for Applicant

Date of Signature: August 6, 2007